Remarks

A. Summary of the Invention.

The instant application relates to a fragment of the product of the *Drosophila* short gastrulation gene (Sog). This particular fragment has an unexpectedly high level of Dpp inhibitory activity as compared to the intact, wild-type protein.

B. Status of the Claims.

Claims 1-26 were pending before this communication. Claims 3-26 have been withdrawn as being drawn to a nonelected invention. Claim 1 is rejected under 35 U.S.C. § 112, and claim 2 is objected to as being dependent on rejected claim 1. No claim amendments have been made by the present response. The specification has been amended to correct typographical errors and to comply with sequence requirements. These amendments add no new matter as they are fully supported by the specification and the original claims, and are merely provided to clarify the subject matter of the present invention. Attached hereto is a marked-up version of the changes made to the specification, labeled APPENDIX A.

Accordingly, claims 1 and 2 are currently under consideration. For the Examiner's convenience, a clean copy of these claims is also provided in APPENDIX B.

C. Entry of the Substitute Specification under 37 C.F.R. § 1.125.

Applicants respectfully request that the previously presented substitute specification filed January 11, 2002 not be entered. In lieu thereof, replacement paragraphs are being presented by the present response to correct typographical errors and to comply with sequence requirements.

D. Sequence Compliance with 37 C.F.R. § 1.821-1.825.

Upon entry of the present amendment, all of the instances of "SEQ.ID.No." have been corrected to "SEQ ID NO:" in the replacement paragraphs as requested by the Examiner. In addition, the SEQ ID NOs have been corrected to correspond to the sequence listing previously filed on December 22, 2000 (Paper No. 11). Thus, Applicants respectfully submit that the

application is fully in compliance with the sequence rules, specifically 37 C.F.R. § 1.821(d) pertaining to sequence identifiers in the specification.

E. New Matter Objections.

Applicants respectfully traverse the Examiner's objection to the amendment filed December 22, 2000 (Paper No. 11, response to the notice to comply with sequence requirements) under 35 U.S.C. § 132 because it allegedly introduces new matter into the disclosure.

Applicants respectfully traverse the Examiner's objection to the amendment filed January 11, 2002 (Paper No. 16, providing formal drawings) under 35 U.S.C. § 132 because it allegedly introduces new matter into the disclosure.

Concerning both of these objections, Applicants respectfully submit that neither the sequence listing nor the formal drawing constitute new matter as defined by the MPEP and the courts. "Matter **not** in the original specification , claims, or drawings is usually new matter." Emphasis added, MPEP § 608.04(a). To the contrary, both the sequence listing and the drawings merely replicate the exact content of Figures 1-6 as filed with the original specification as follows:

SEQ ID NO:	Original Figure
1	1; nucleic acid
2	1; amino acid
3	2; nucleic acid
4	2; amino acid
5	3; nucleic acid
6	3; amino acid
7	4; nucleic acid
8	4; amino acid
9	5; amino acid
10	5; amino acid
11	6; nucleic acid
12	6; amino acid

Applicants respectfully submit that an amendment to a specification does not violate the new matter rule if it merely clarifies or completes the original disclosure (see, e.g., *In re* Wright, 145 USPQ 182 (CCPA 1965)). Both the sequence listing and the formal drawings are fully supported by the originally filed informal drawings. Not one change has been made to the drawings or the sequences contained therein. The fact that the drawings may be difficult to read has been remedied by the clarification provided by the formal set of drawings submitted. Applicants respectfully submit that the sequences could not have been illegible or unreadable, since they were easily retyped by a word-processor, having no technical background, in the preparation of the formal drawings. In the interests of justice, Applicants should not be penalized for providing a poor photocopy of the drawings, which were indeed submitted as informal drawings.

Accordingly, Applicants respectfully request reconsideration of both the objection to the sequence listing and the objection to the formal drawings prior to filing a Petition to the Commissioner under 37 C.F.R. § 1.181.

F. 35 U.S.C. § 112 Rejection.

The rejection of claim 1 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey that Applicants had possession of the claimed invention, is respectfully traversed. The Examiner has alleged that support for the limitation "synthetic" cannot be found in the specification or claims as originally claimed (see Office Action mailed January 22, 2002, at page 4, paragraph 5). Applicants respectfully submit that the specification explicitly contemplates preparation of Super-Sog that has been "synthesized chemically" (see specification at page 6, lines 16-18).

Furthermore, "expression of a polynucleotide sequence which encodes Super-Sog" using all methods that are well known in the field (see, e.g., specification at page 7, lines 14-21), clearly covers any form of polynucleotide that could be used and subcloned into an expression vector, including a synthetic polynucleotide comprising the sequences identified by the

Applicants. Therefore, one of skill in the art would have no reason to doubt that Applicants had possession of a synthetic polynucleotide based on the sequences provided.

Moreover, the introduction of a term that simply makes explicit that which was inherent or implicit in the original disclosure does not constitute new matter. The specification as filed clearly support the option of expressing the Super-Sog protein using a synthetic polynucleotide encoding the same. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

Conclusion

In view of the above amendment and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved in view of this communication, the Examiner is encouraged to call the undersigned so that a prompt disposition of this application can be achieved.

Respectfully submitted,

Date: May 22, 2002

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Enclosures: Appendices A and B

APPENDIX A – ALTERED SPECIFICATION

VERSION WITH MARKINGS TO SHOW CHANGES MADE

The paragraph beginning at page 3, line 1, has been amended as follows:

-- The invention therefore provides Super-Sog (**SEQ ID NO:2** [~~**SEQ.ID.No. 1**~~]; amino acids 1-292 of Sog) and active variants thereof. Such variants include **SEQ ID NO:4** [~~**SEQ.ID.No. 3**~~], a recombinant Super-Sog peptide which includes 33 amino acids encoded by the pUAS expression vector; **SEQ ID NO:6** [~~**SEQ.ID.No. 6**~~], a Super-Sog peptide which includes a mutation (W A) in the CR-1 sequence; and **SEQ ID NO:8** [~~**SEQ.ID.No. 7**~~], a Super-Sog peptide which terminates 5' of the CR-1 sequence. Such variants also include Super-Sog with 5' modifications, such as modifications to the Tolloid protease cleavage site, addition of other peptides and inclusion of additional 5' regions of Sog (e.g., CR-2). --

The paragraph beginning at page 3, line 23, has been amended as follows:

-- FIGURE 1 is a diagram of the nucleotide sequence (**SEQ ID NO:1** [~~**SEQ.ID.No. 1**~~]) coding for a Super-Sog polypeptide, whose amino acid sequence (**SEQ ID NO:2** [~~**SEQ.ID.No. 2**~~]) is shown beneath the nucleotide codons in the Figure. Transmembrane (TM) and CR-1 regions of the coding sequence and peptide are indicated in the right margin of the FIGURE. --

The paragraph beginning at page 3, line 28, has been amended as follows:

-- FIGURE 2 is a compilation of the nucleotide sequence [~~(**SEQ.ID.No. 1**)~~] coding for a Super-Sog polypeptide and 33 amino acids encoded by the pUAS expression vector [~~(**SEQ.ID.No. 3**)~~], coded by the nucleotide sequence following the NotI restriction site. **The nucleotide sequence (SEQ ID NO:3) and the amino acid sequence (SEQ ID NO:4) are shown.** --

The paragraph beginning at page 4, line 1, has been amended as follows:

-- FIGURE 3 is the nucleotide sequence (**SEQ ID NO:5** [~~**SEQ.ID.No. 6**~~]) coding for a Super-Sog peptide (**SEQ ID NO:6**) which includes a mutation (W→A) in the CR-1 sequence. --

The paragraph beginning at page 4, line 5, has been amended as follows:

-- FIGURE 4 is the nucleotide sequence (**SEQ ID NO:7** [~~**SEQ.ID.No. 7**~~]) coding for a Super-Sog peptide which is modified 5' of the NotI restriction site sequence of **SEQ ID NO:3** [~~**SEQ.ID.No. 3**~~] (**SEQ ID NO:8**). --

The paragraph beginning at page 4, line 8, has been amended as follows:

-- FIGURE 5 is a line comparison demonstrating partial sequence homology between Super-Sog (**SEQ ID NO:2** [~~**SEQ.ID.No. 4**~~]) and another Dpp antagonist in *Drosophilia*, noggin (**SEQ ID NOs:9** [~~**SEQ.ID.No. 5**~~]). –

The paragraph beginning at page 4, line 11, has been amended as follows:

-- FIGURE 6 is the full-length nucleotide sequence (**SEQ ID NO:11** [~~**SEQ.ID.No. 8**~~]) coding for wild-type Sog **protein (SEQ ID NO:12)**. --

The paragraph beginning at page 5, line 13, has been amended as follows:

-- Given their similarity in structure, it would be reasonably expected that any *Dpp* inhibitory activity conferred on the Sog protein by the CR repeats would be comparable in quality. It was therefore a surprise to find that a peptide encoded by CR-1 (Super-Sog; **SEQ ID NO:2** [~~**SEQ.ID.No. 1**~~]) has greater Dpp inhibitory activity in certain respects than wild-type Sog. --

The paragraph beginning at page 6, line 16, has been amended as follows:

-- Super-Sog is prepared as a purified peptide fragment from Sog (e.g., **SEQ ID NO:2** [~~**SEQ.ID.No. 2**~~]), expressed as a recombinant peptide using, for example, the coding sequences set forth in **SEQ ID NOs:1, 3, 5 or 7** [~~**SEQ.ID.Nos. 1, 3, 6 or 7**~~], or synthesized chemically. Techniques for production of peptides according to each of these methods are well-known in the art and so will only be described briefly here. --

The paragraph beginning at page 7, line 14, has been amended as follows:

-- Recombinant Super-Sog can also be produced *in vitro* or *in vivo* through expression of a polynucleotide sequence which encodes Super-Sog (e.g., **SEQ ID NO:1** [~~**SEQ.ID.No. 1**~~]). In general, prokaryotes are used for cloning of DNA sequences in constructing recombinant expression vectors. For example, *E. coli* K12 strain 294 (ATCC Accession No. 31446) may be particularly useful. Prokaryotes also are used for expression. The aforementioned strain, as well as *E. coli* W3110 (ATTC Accession No. 27325), bacilli such as *Bacillus subtilus*, and other enterobacteriaceae such as *Salmonella typhimurium* or *Serratia marcescans*, and various *pseudomonas* species may also be used for expression. --

The paragraph beginning at page 21, line 4, has been amended as follows:

-- **SEQ ID NO:1** [~~**SEQ.ID.No. 1**~~] is the nucleotide sequence which codes for a Super-Sog polypeptide. --

The paragraph beginning at page 21, line 6, has been amended as follows:

-- **SEQ ID NO:2** [~~**SEQ.ID.No. 2**~~] is the predicted amino acid sequence of Super-Sog **encoded by SEQ ID NO:1** [~~**based on SEQ.ID.No. 1**~~]. --

The paragraph beginning at page 21, line 8, has been amended as follows:

-- **SEQ ID NO:3** [~~**SEQ.ID.No. 3**~~] is a compilation of the nucleotide sequence [~~**(SEQ.ID.No. 1)**~~] coding for a Super-Sog polypeptide and 33 amino acids of the pUAS expression vector [~~**(SEQ.ID.No. 3)**~~], coded by the nucleotide sequence following NotI. --

The paragraph beginning at page 21, line 12, has been amended as follows:

-- **SEQ ID NO:4** [~~**SEQ.ID.No. 4**~~] **is the predicted amino acid sequence encoded by SEQ ID NO:3** [~~**is a partial nucleotide sequence for *Super* Sog encompassing a region of homology to *noggin***~~]. --

The paragraph beginning at page 21, line 15, has been amended as follows:

-- **SEQ ID NO:10** [~~**SEQ.ID.No. 5**~~] is a partial **amino acid** [~~**nucleotide**~~] sequence for *noggin* encompassing a region of homology to *Super-Sog*. **SEQ ID NO:9 is the full-length *noggin* amino acid sequence.** --

The paragraph beginning at page 21, line 18, has been amended as follows:

-- **SEQ ID NO:5** [~~**SEQ.ID.No. 6**~~] is the nucleotide sequence coding for a Super-Sog peptide which includes a mutation (W→A) in the CR-1 sequence **(SEQ ID NO:6)**. --

The paragraph beginning at page 21, line 21, has been amended as follows:

-- **SEQ ID NO:7** [~~**SEQ.ID.No. 7**~~] is the nucleotide sequence coding for a Super-Sog peptide which is modified 5' of the NotI restriction site sequence of **SEQ ID NO:3** [~~**SEQ.ID.No. 3**~~] **(SEQ ID NO:8)**. --

The paragraph beginning at page 21, line 24, has been amended as follows:

-- **SEQ ID NO:11** [~~**SEQ.ID.No. 8**~~] is the full-length nucleotide sequence coding for wild-type Sog **(SEQ ID NO:12)**. --